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1/59

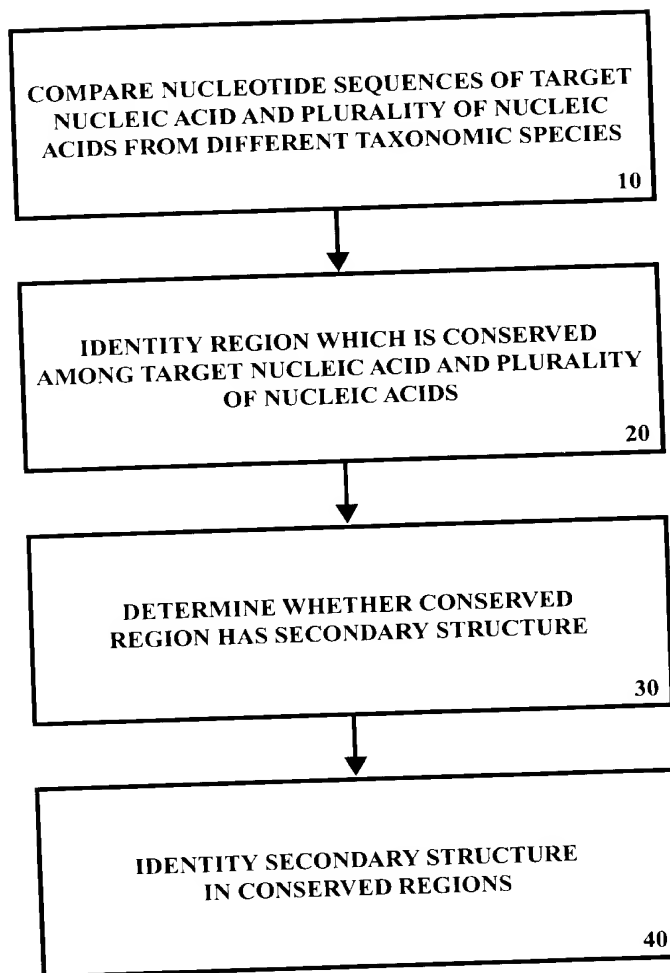


FIGURE 1



2/59

**Find Neighbors
and Assemble
Flow Diagram**

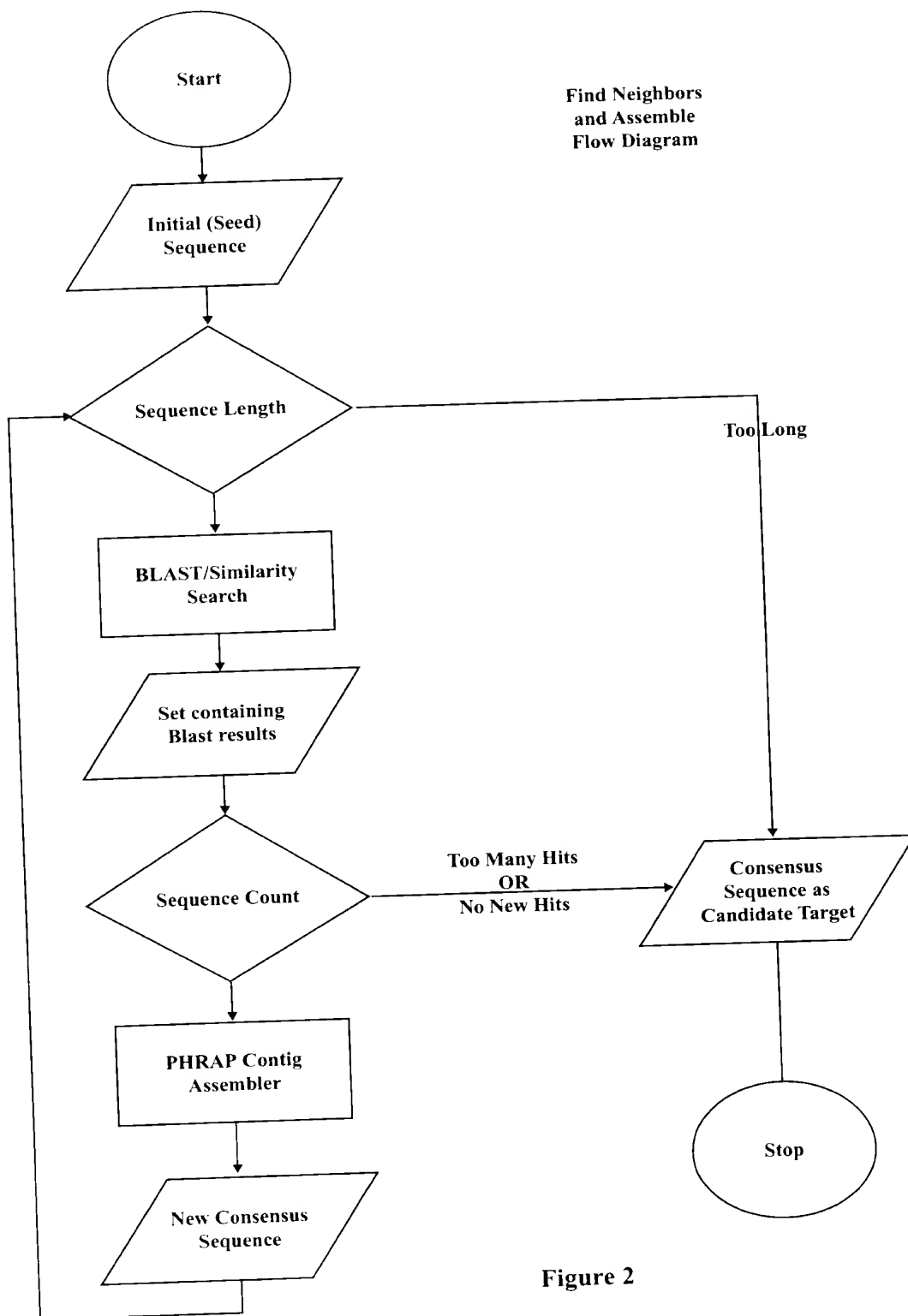
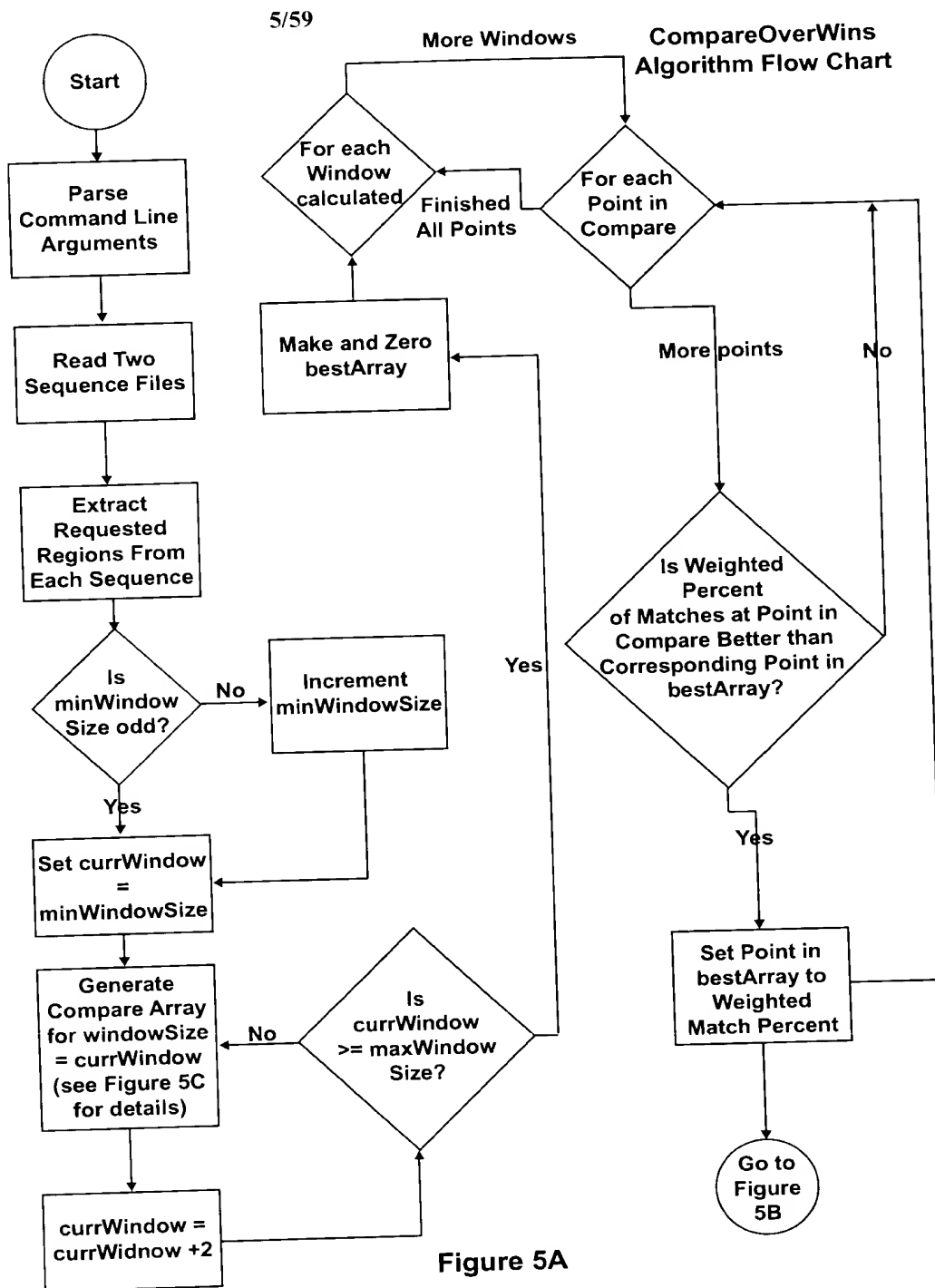


Figure 2





13/59

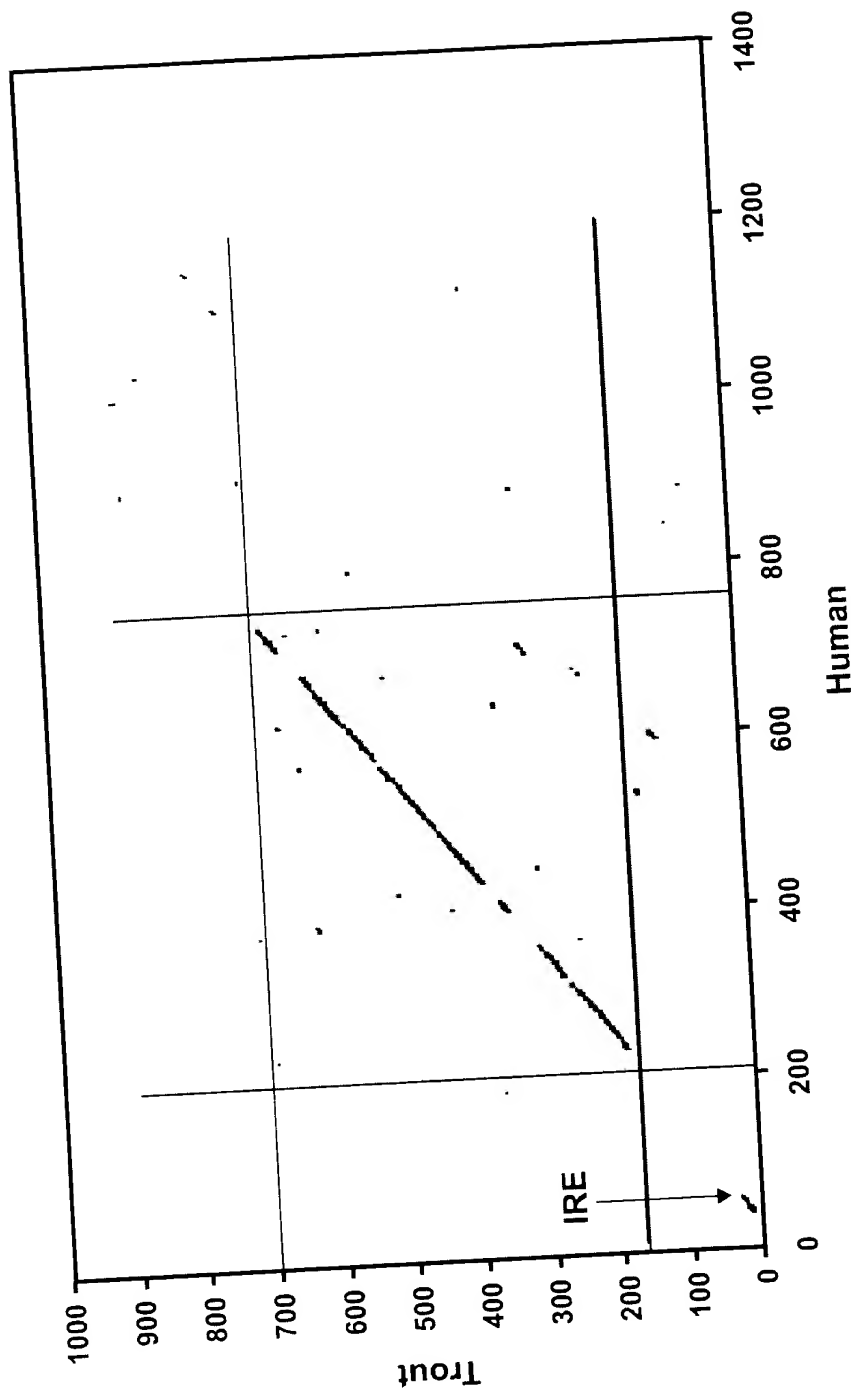


Figure 11



14/59

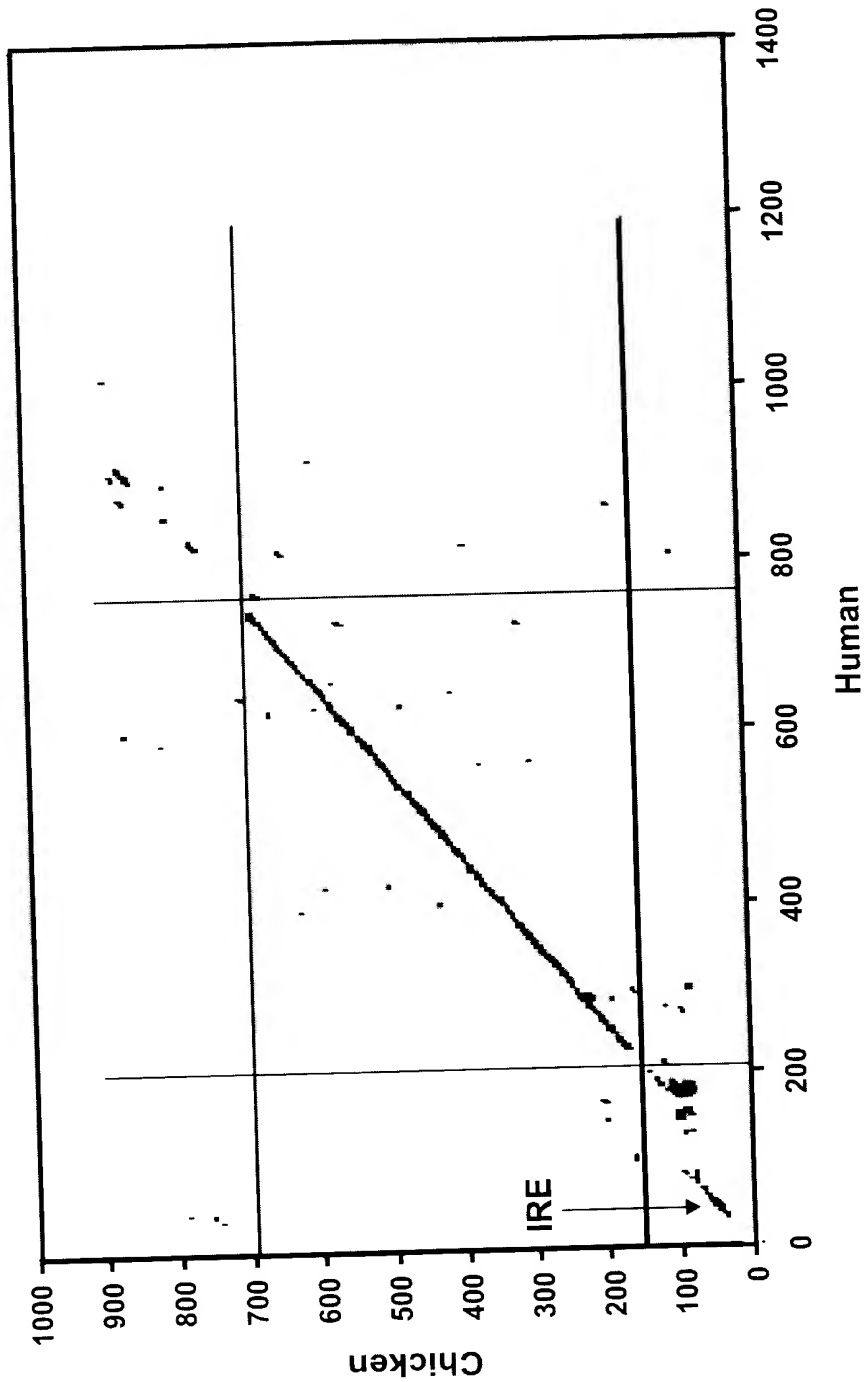


Figure 12



15/59

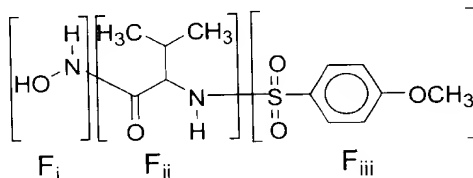
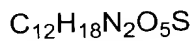
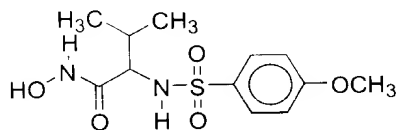
	HUMAN PIG	HAMSTER MOUSE RAT	CHICKEN	TROUT SALMON	XENOPUS FROG	FLY	MOSQUITO
	GU A G C C	GU A G C C	GU A G C C	GU A G C C	GU A G C C	GU A G C C	GU A G C C
	A-U A-U C-G U-G U-A C	A-U A-U C-G U-A U-A C	A-U A-U C-G U-G G-A C	A-U A-U C-G U-A U-A C	A-U A-U C-G U-A U-A C	A-U A-U C-G U-A U-A C	A-U A-U C-G U-A U-A C
	G-C U-G C-G	G-C U-G C-G	G-C U-G C-G	G-C U-G U-G	G-C U-G U-G	U-A U-A C-G	U-A U-A C-G
HUMAN PIG	NO	NO	YES	YES	YES	NO	NO
HAMSTER MOUSE RAT		NO	YES	YES	YES	NO	NO
CHICKEN			NO	YES	YES	NO	NO
TROUT SALMON				NO	YES	YES	YES
XENOPUS FROG					NO	YES	YES
FLY						NO	YES
MOSQUITO							NO

Figure 13



16/59

Compound CI



Molecular Formula

H_2NO

C_5H_9NO

$C_7H_7O_3S$

Figure 14

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17/59

Addition of fragments to yield compounds

Table

Fragment Identifier	Structure	Name	Molecular formula	Other
F _i		Hydroxylamine	H ₂ NO	...
F _{ii}		Amino acid	C ₅ H ₉ NO	...
F _{iii}		Sulfonyl	C ₇ H ₇ O ₃ S	...

Figure 15



18/59

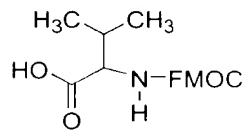
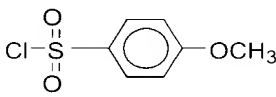
Reagents	Identifier	Name	Properties
$\text{H}-\text{O}-\text{NH}_2$ or $\textcircled{\text{P}}-\text{O}-\text{NH}_2$	R_i	Hydroxylamine	...
	R_{ii}	FMOC blocked amino acid	...
	R_{iii}	Sulfonylchloride	...
$\textcircled{\text{P}}$ = solid support			

Figure 16

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19/59

Transformation

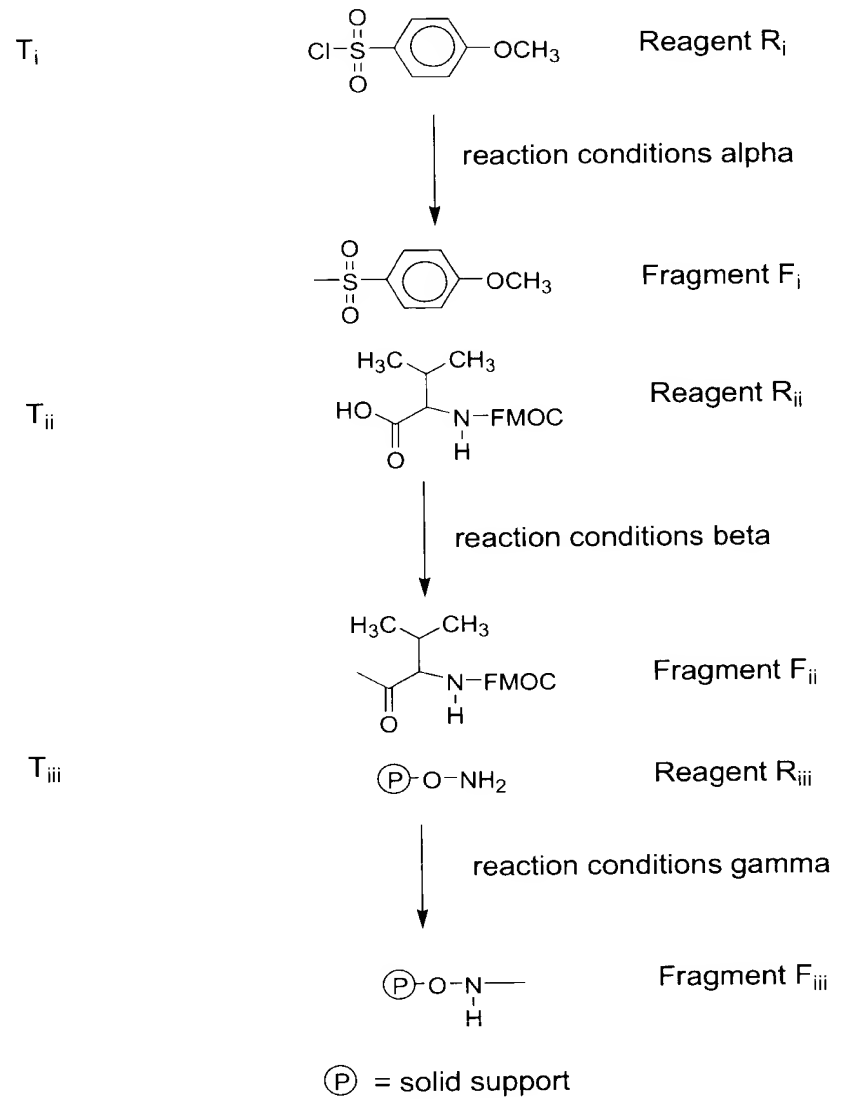


Figure 17



20/59

Common Fragment/Different Reagents and Transformations

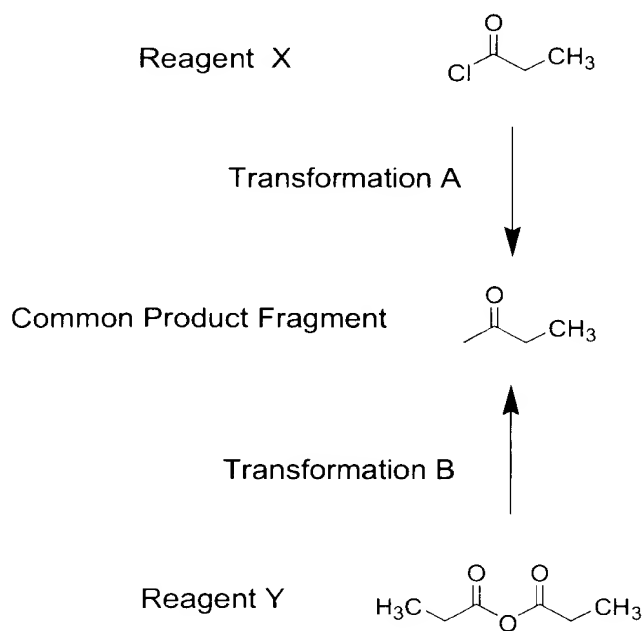
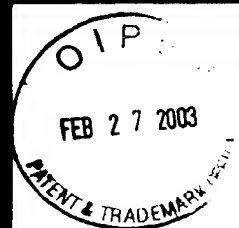


Figure 18



21/59

Common Fragment/Different Reagents and Transformations

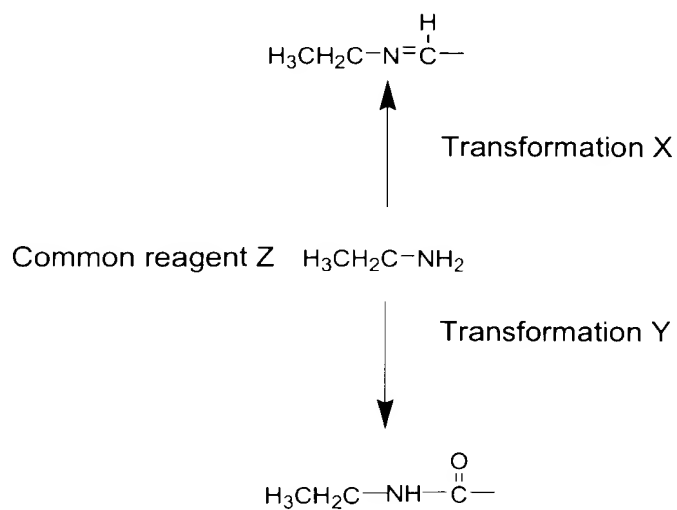


Figure 19A



22/59

Common Reagent

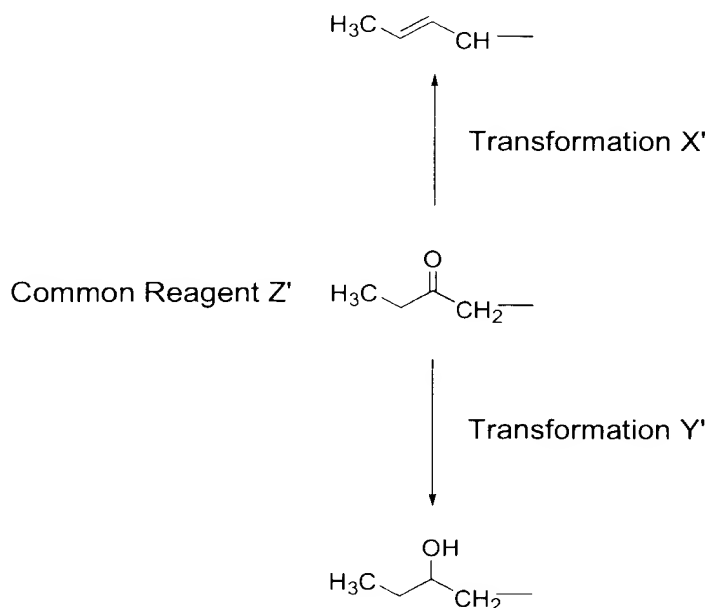


Figure 19B



23/59

Symbolic addition of fragments to yield compound

<u>Symbolic Structure</u>	<u>Symbolic Identifier</u>	<u>Molecular formula</u>
---------------------------	----------------------------	--------------------------

Fragment



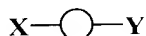
F_i'

C_uH_vN_w ...



F_{ii}'

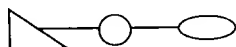
C_uH_vN_w ...



F_{iii}'

C_uH_vN_w ...

Compound



CI'

C_uH_vN_w ...

Molecular formula F_i'

+

Molecular formula F_{ii}'

+

Molecular formula F_{iii}'

= Molecular formula CI'

Figure 20

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24/59

Symbolic Reagent Table

<u>Identifier</u>	<u>Name</u>	<u>Structure</u>	<u>Molecular formula</u>
R1	xxx		xxx
R2
R3
R4
R5
R6
R7
R8
R9
R10

Figure 21



25/59

Symbolic Fragment Table



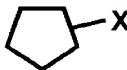
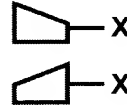


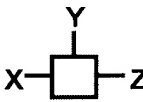
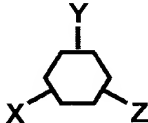
<u>Identifier</u>	<u>Symbolic Sturcture</u>	<u>Molecular Formula</u>	<u>Molecular Weight</u>
F1		XXX	XXX
F2	
F3	
F4	
F5	
F6	
F7	
F8	

Figure 22



26/59

Symbolic Transformation Table



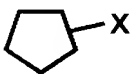
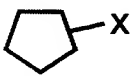
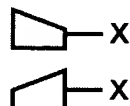



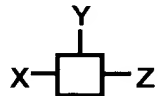
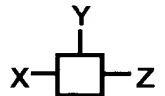
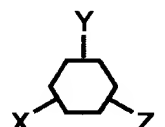
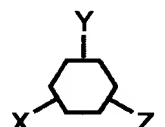
Identifier		Symbolic Reactions		Reagent
T1	F1	 X	← R1	conditions α
T2	F2	 X	← R2	conditions β
T3	F3	 X	← R3	conditions α
T4	F3	 X	← R4	conditions α
T5	F4	 X	← R5	conditions α
T6	F5	X-  Y	← R6	conditions ε
T7	F5	X-  Y	← R7	conditions α
T8	F6	X-  Y	← R8	conditions α
T9	F7	 Y X-  Z	← R9	conditions γ
T10	F8	 Y X-  Z	← R10	conditions γ

Figure 23



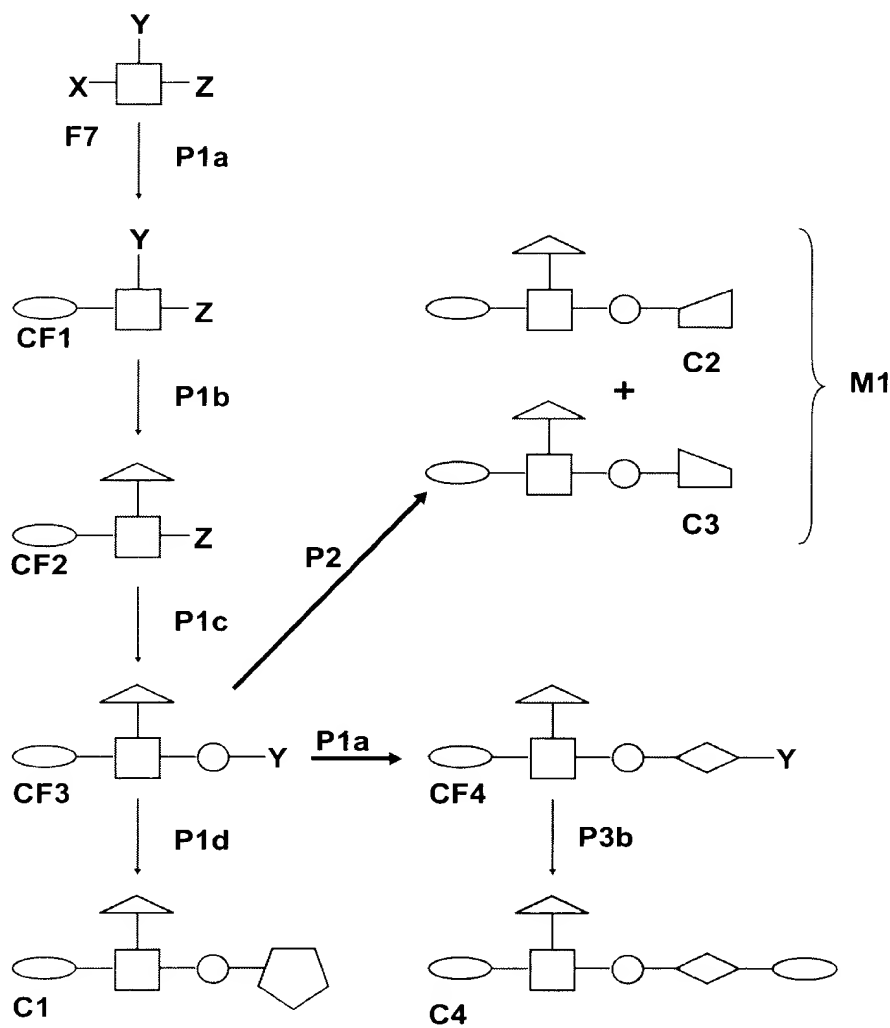
27/59

Single Compounds and Mixtures

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P = synthetic path
F = fragment
C = compound
CF = complex fragment
M = mixture

Figure 24

28/59

Mixture 2

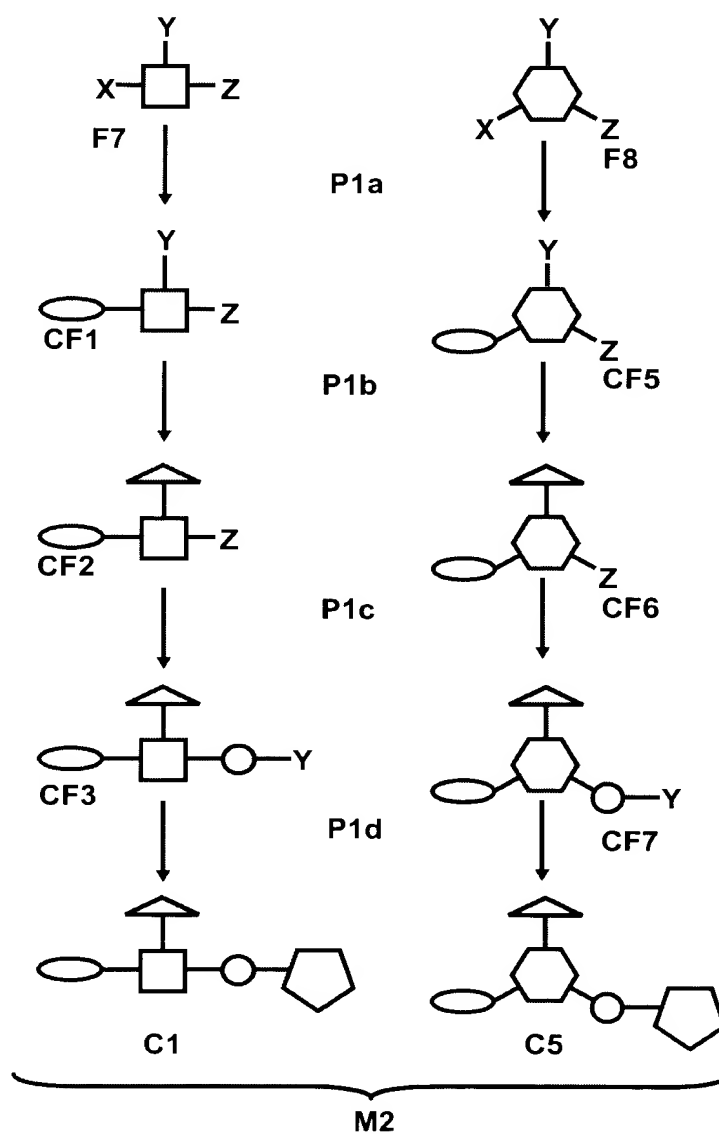


Figure 25



29/59

Mixture 3

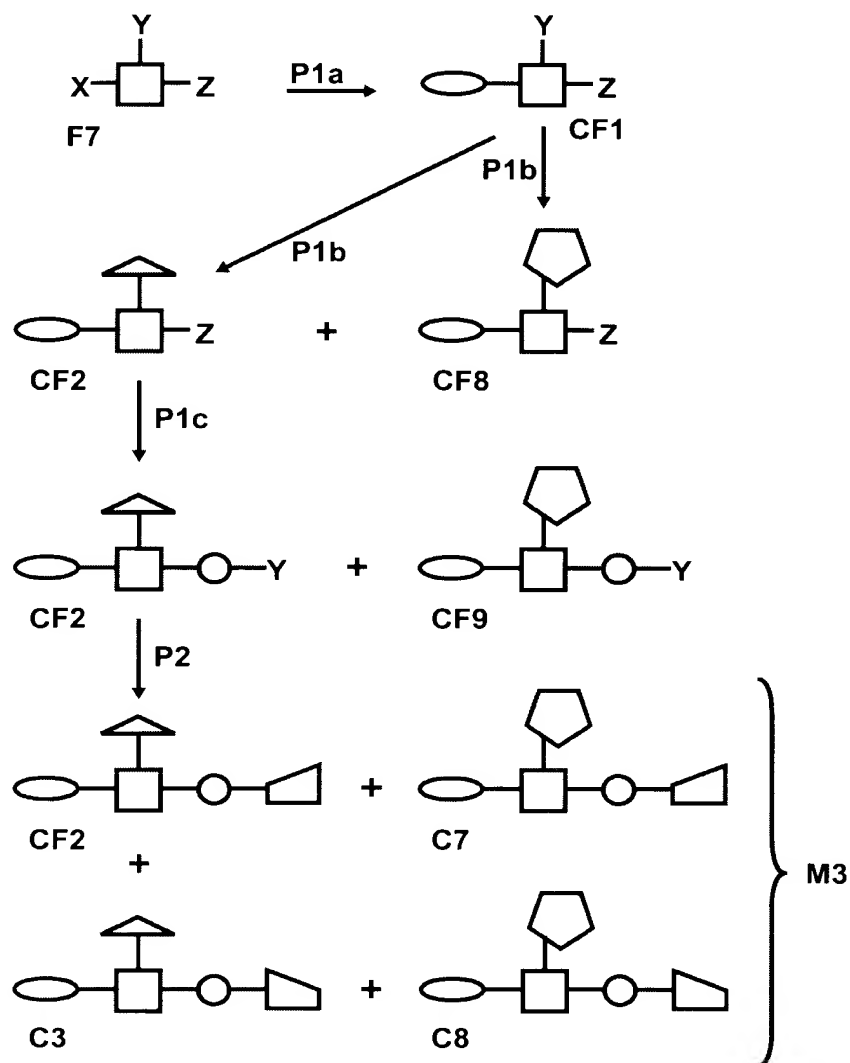


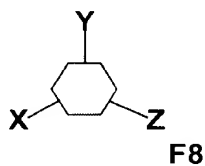
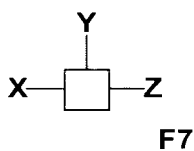
Figure 26



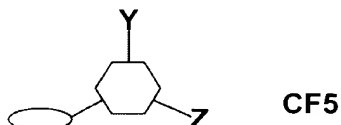
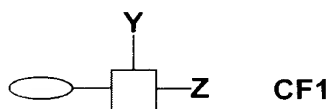
30/59

Mixture 4

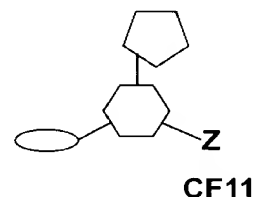
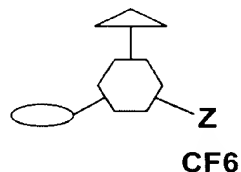
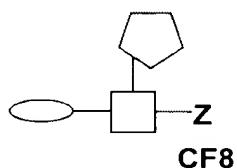
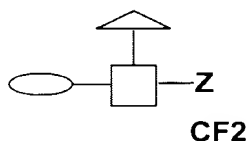
2 Starting Fragments



2 Complex Fragments



4 Complex Fragments



8 Complex Fragments

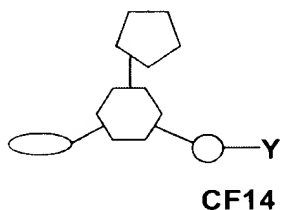
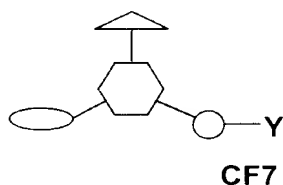
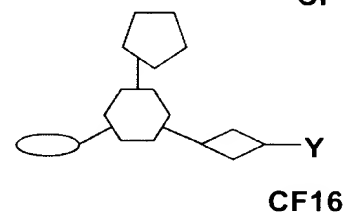
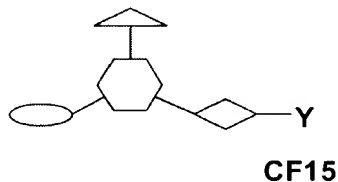
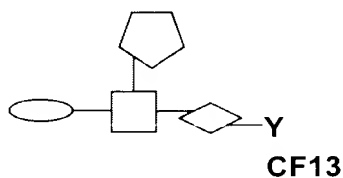
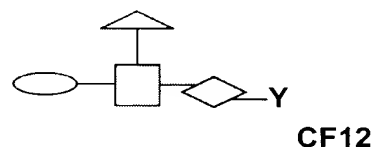
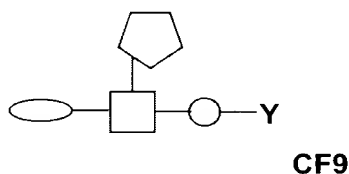
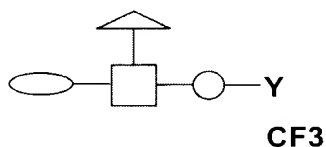


Figure 27A

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31/59

Mixture 4 (continued)

16 compounds

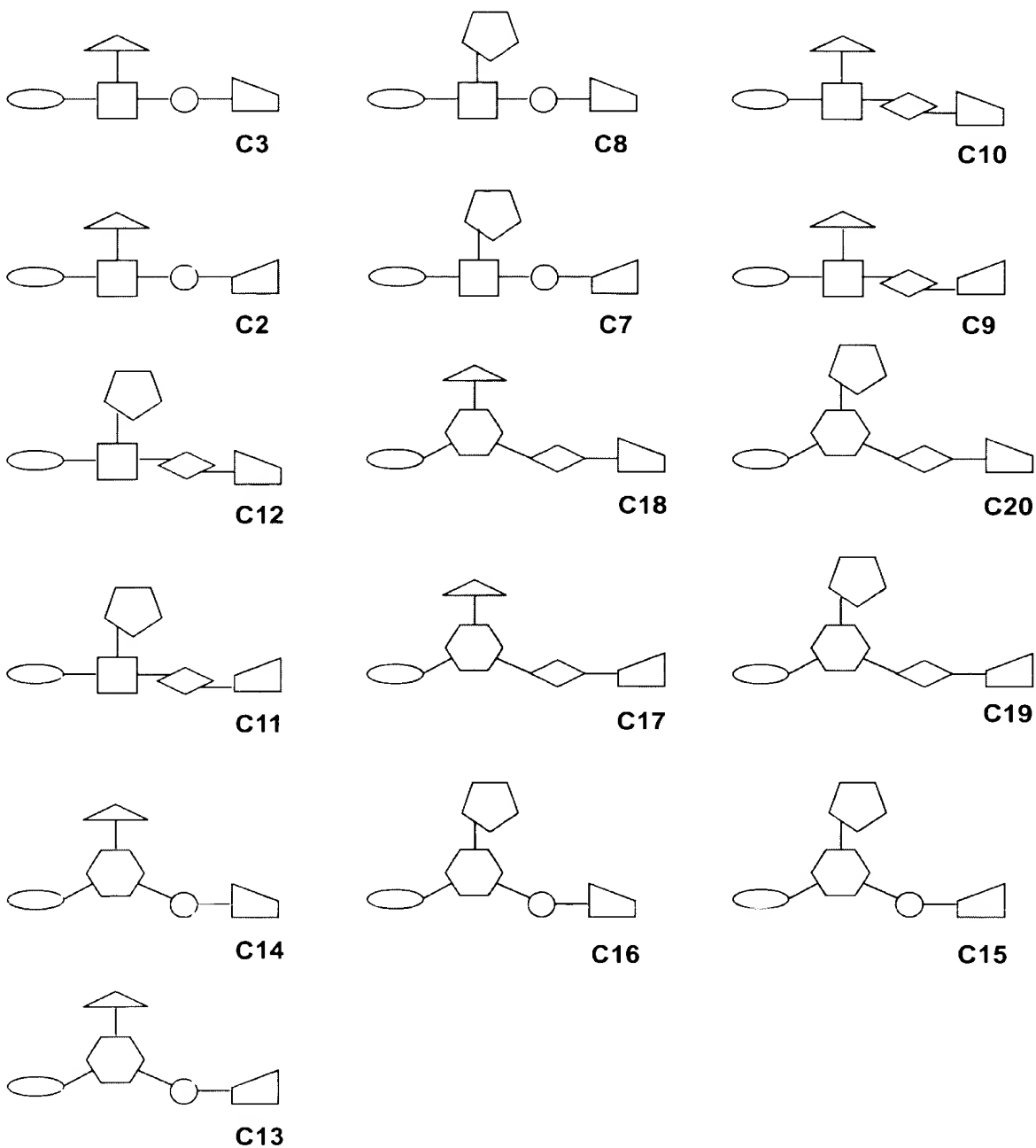


Figure 27B



32/59

Tracking Table for Compound C1

(a) By Fragments:

n	n+1	n+2
F7	F2 F1 F5	F3

(a) By Transformations:

Synthesis Path 1

n	n+1	n+2
T9	T2 T1 T6	T3

Synthesis Path 2

n	n+1	n+2
T9	T2 T1 T7	T3

Synthesis Path 3

n	n+1	n+2
T9	T2 T1 T6	T4

Synthesis Path 4

n	n+1	n+2
T9	T2 T1 T7	T4

Figure 28



33/59

Tracking Table

Tracking M1

Step 1		
T9		
Step 2		
T9	T2	
Step 3		
T9	T2 T1	
Step 4		
T9	T2 T1 T7	
Step 5		
T9	T2 T1 T7	T5 ¹
C2		
Step 5		
T9	T2 T1 T7	T5 ²
C3		

Figure 29



34/59

Tracking Table

Tracking M2

Step 1		
n	n+1	n+2
T9		

Step 2		
n	n+1	n+2
T9	T2	

Step 3		
n	n+1	n+2
T9	T2 T1	

Step 4		
n	n+1	n+2
T9	T2 T1 T7	

Step 5		
n	n+1	n+2
T9	T2 T1 T7	T4

C1

Step 1		
n	n+1	n+2
T10		

Step 2		
n	n+1	n+2
T10	T2	

Step 3		
n	n+1	n+2
T10	T2 T1	

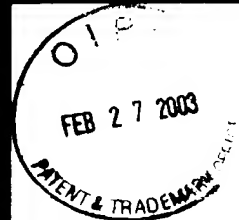
Step 4		
n	n+1	n+2
T10	T2 T1 T7	

Step 5		
n	n+1	n+2
T10	T2 T1 T7	T4

C5

Figure 30

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35/59

Tracking Table

Tracking M3

Step 1

T9		
----	--	--

Step 2

T9	T2	
----	----	--

Step 3

T9	T2 T1	
----	----------	--

Step 3

T9	T2 T3	
----	----------	--

Step 4

T9	T2 T1 T7	
----	----------------	--

Step 4

T9	T2 T3 T7	
----	----------------	--

Step 5

T9	T2 T1 T7	T5 ¹
----	----------------	-----------------

C2

Step 5

T9	T2 T1 T7	T5 ²
----	----------------	-----------------

C3

Step 5

T9	T2 T3 T7	T5 ¹
----	----------------	-----------------

C7

Step 5

T9	T2 T3 T7	T5 ²
----	----------------	-----------------

C8

Figure 31

OIP

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36/59

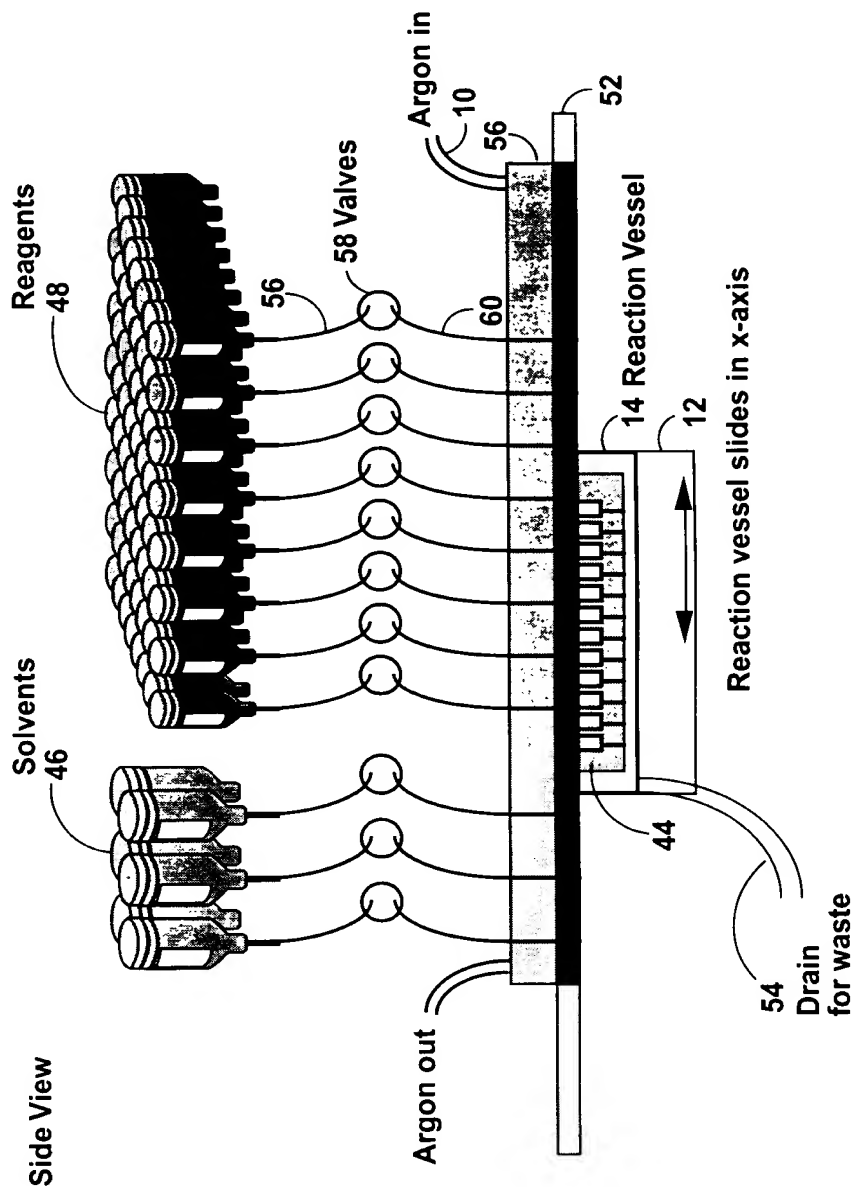


Figure 32

37/59

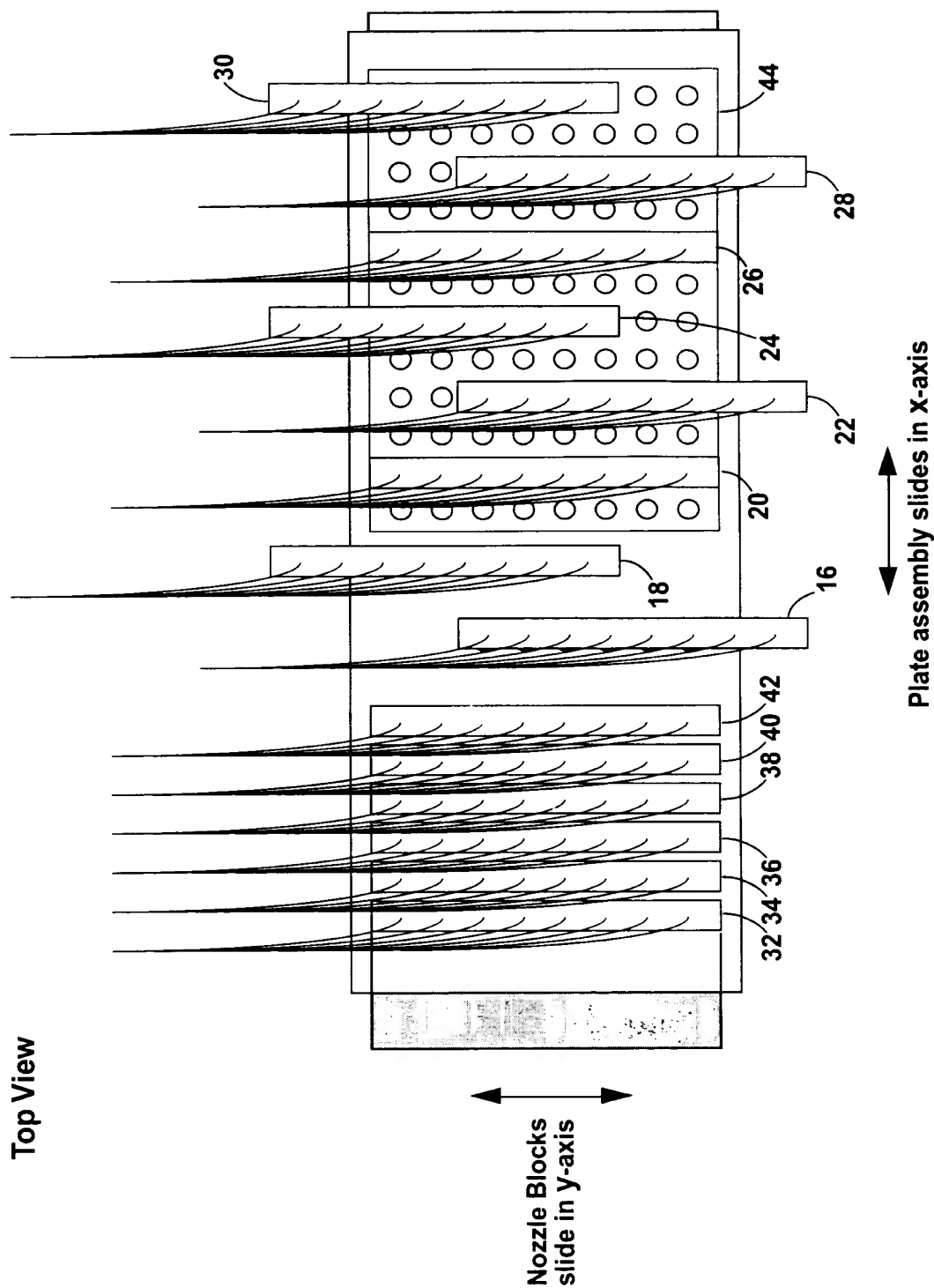


Figure 33



38/59

Synthesis of Hydroxamic acids from alcohol resin

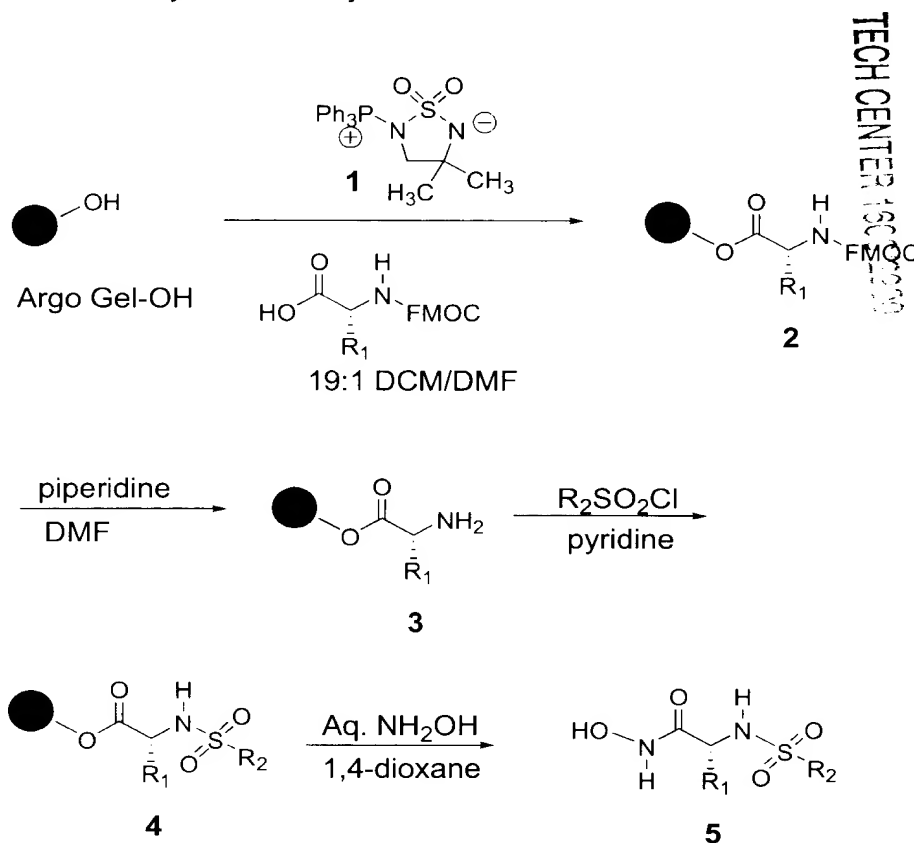


Figure 34

39/59

Synthesis of hydroxylamine resin

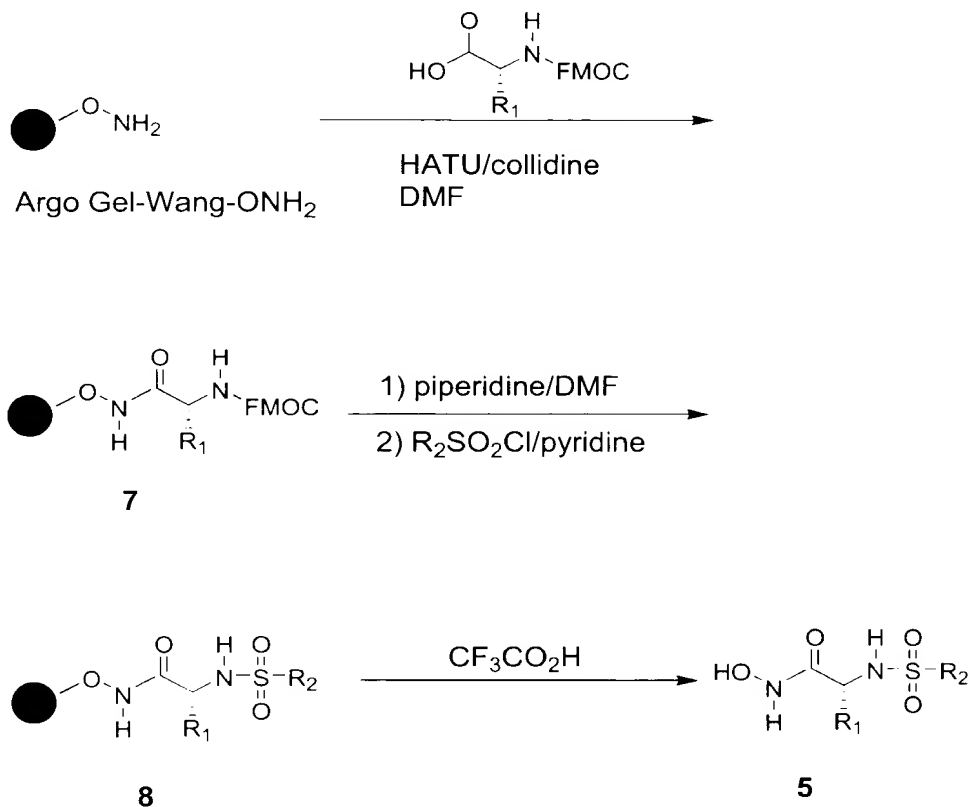


Figure 35



40/59

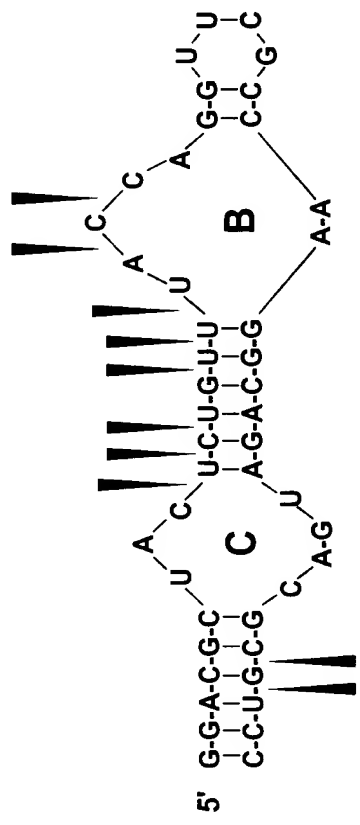


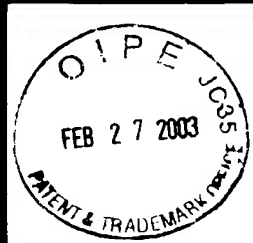
Figure 36



41/59

ACD Code	Structure	Calc. ΔG of binding (kcal/mole)	IC ₅₀ (μM)
00001199		-5.1	< 2
00192509		-8.5	< 2
00003934		-5.1	< 50

Figure 37



42/59

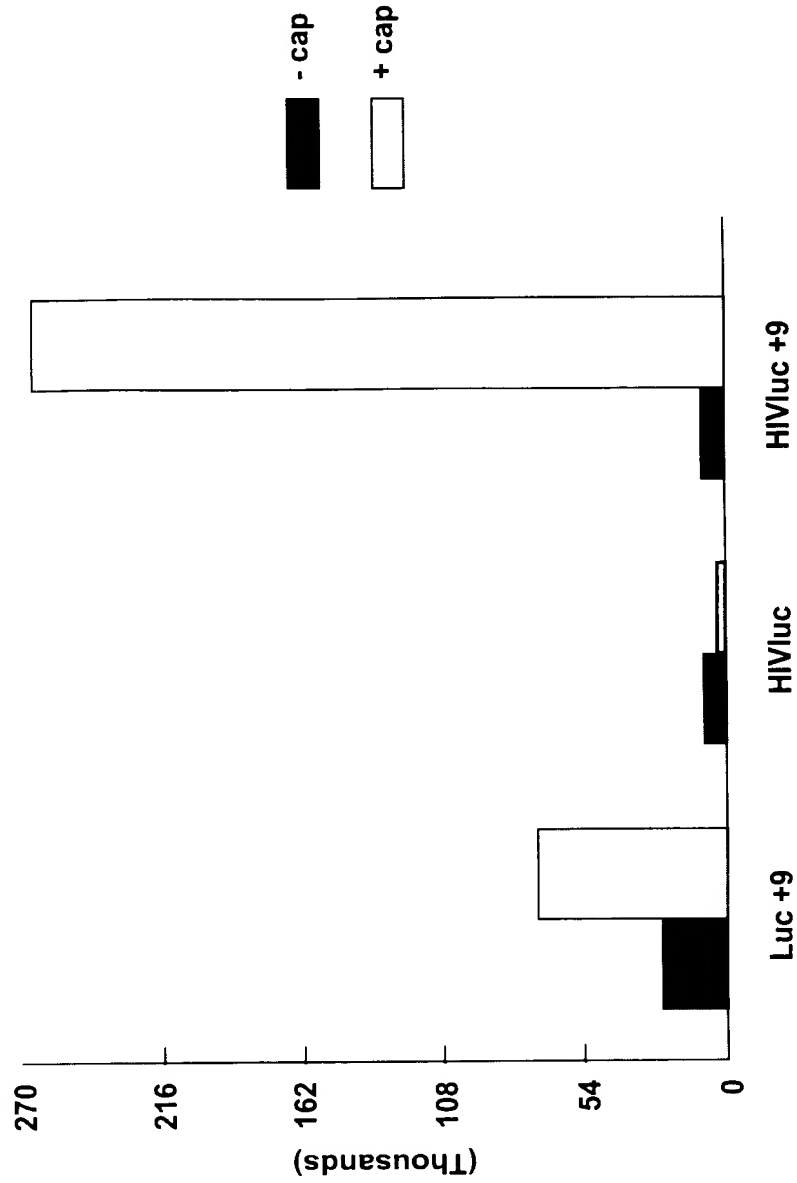
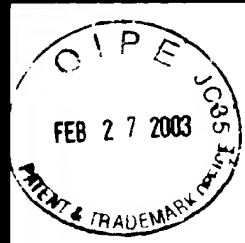


Figure 38A



43/59

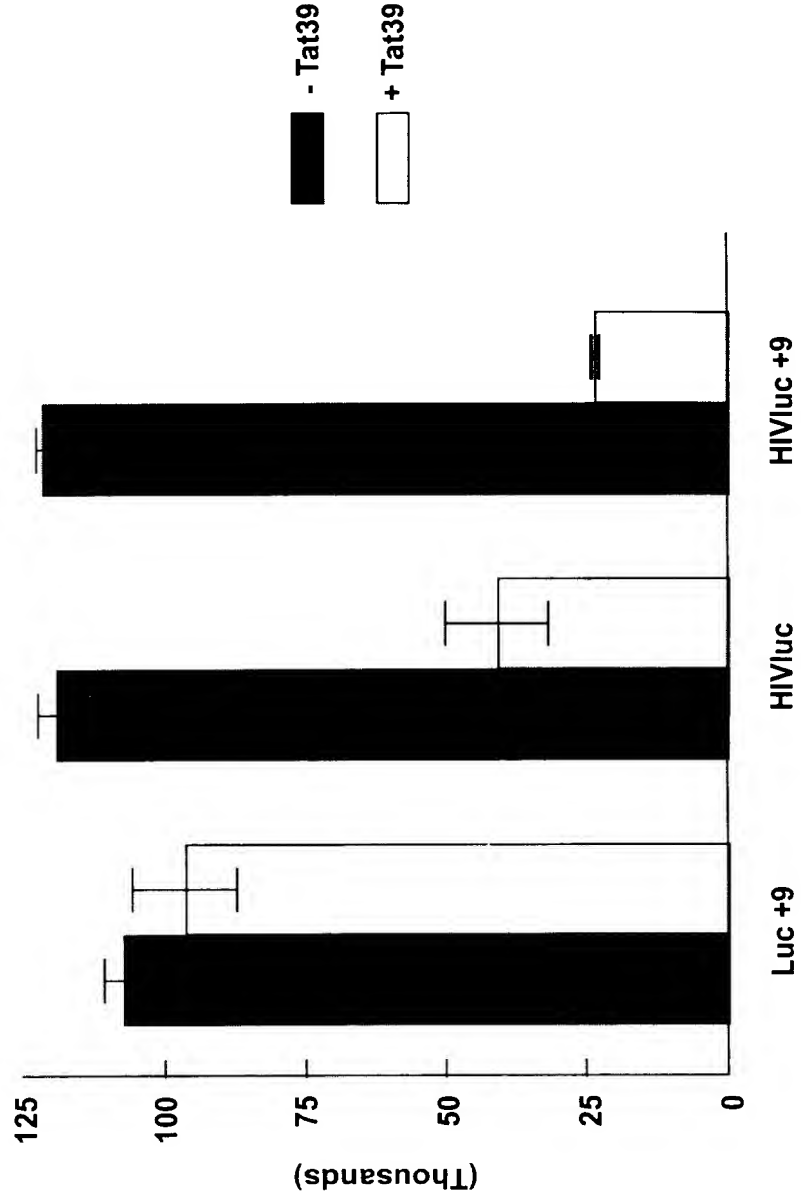


Figure 38B



44/59

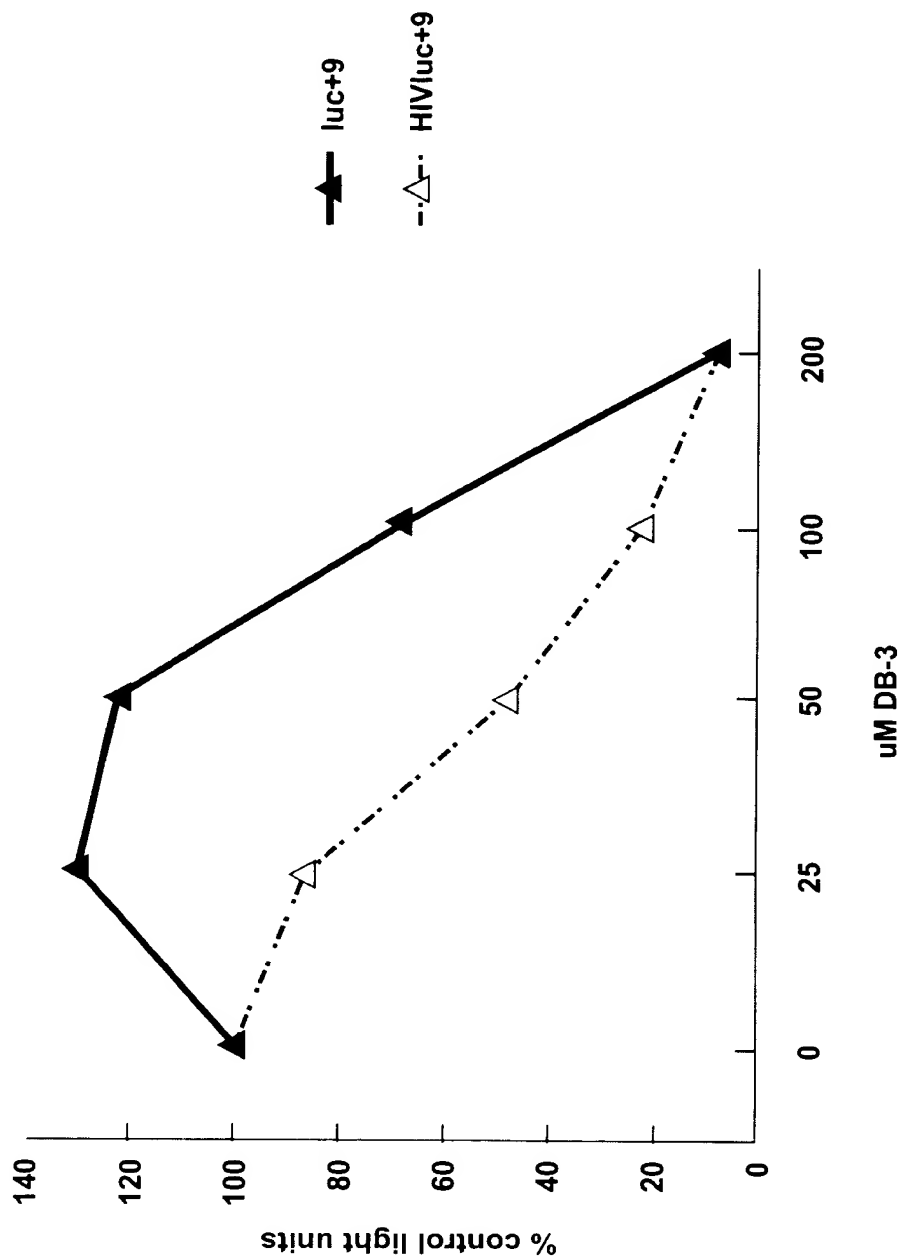


Figure 39

46/59

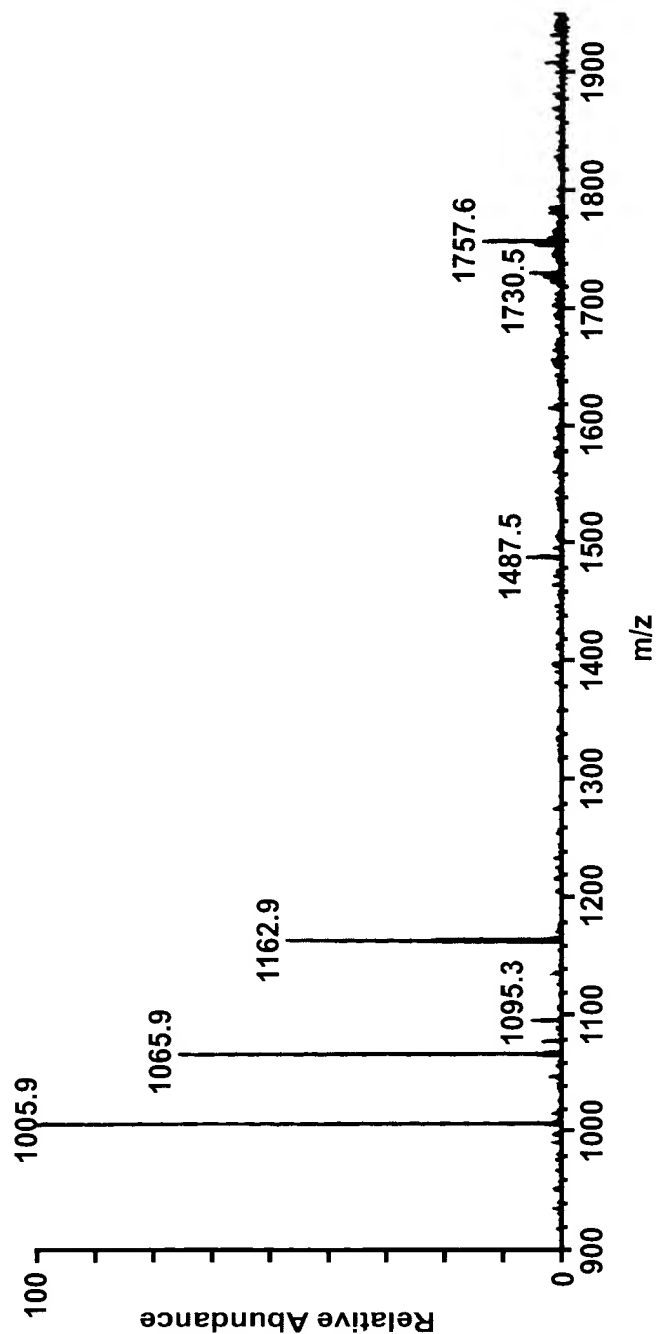


Figure 41A

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Docket No. IBIS-0007
App. No. 09/076,404
Filed May 12, 1998
Title: Identification of Molecular Interaction Sites on RNA and Other Biomolecules
Inventors: Ecker et al.
Attorney: Jeffrey H. Rosedale
Sheet 47 of 59
Phone: (215) 568-3100

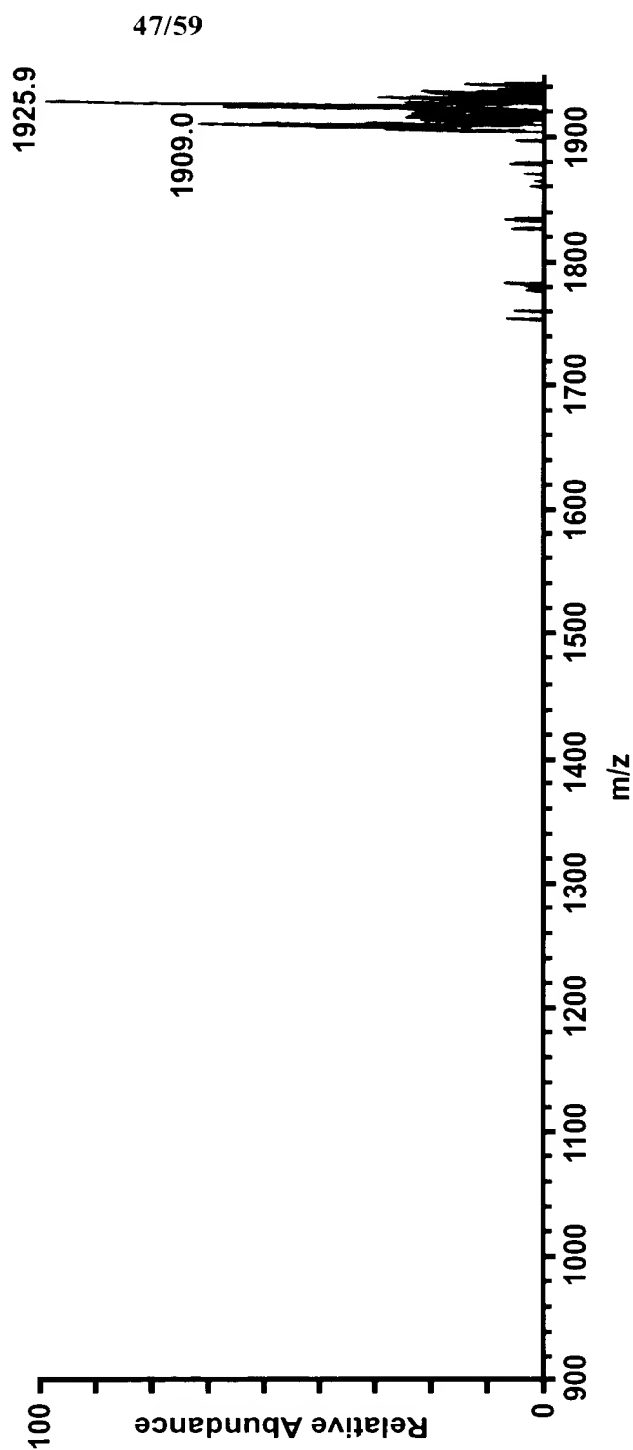


Figure 41B



48/59

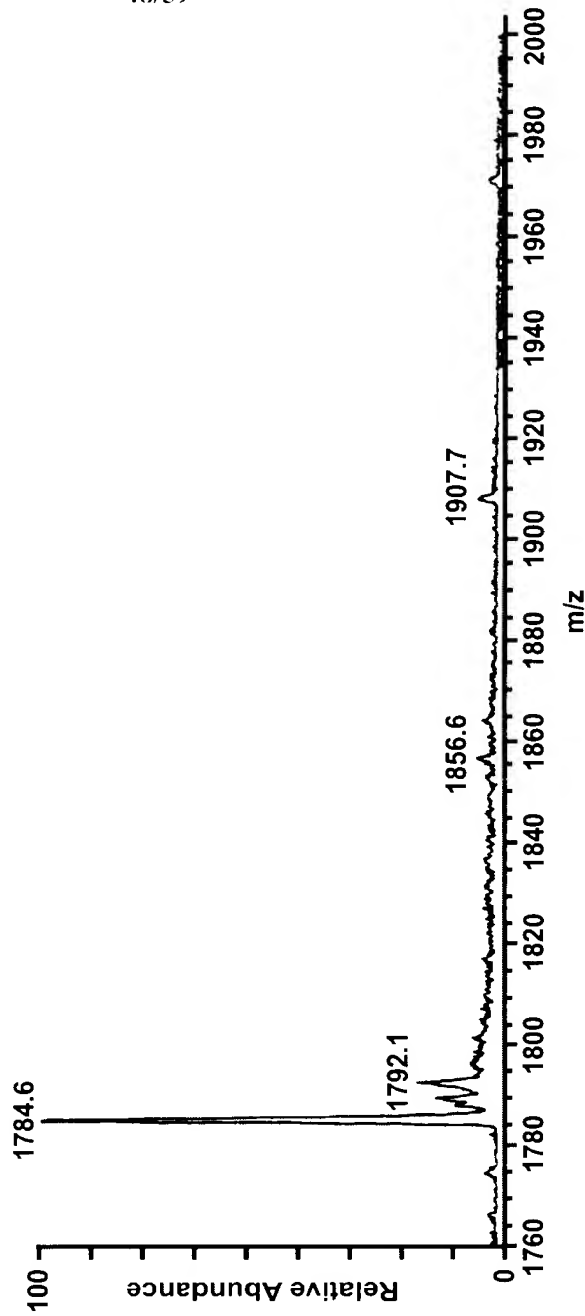


Figure 42A

O I P
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Doc. No.: IBIS-0007
Appl. No.: 09/076,404
Filed: May 12, 1998
Title: Modulation of Molecular Interaction Sites on RNA and Other Biomolecules
Inventors: Ecker et al.
Attorney: Jeffrey H. Rosedale
Sheet 49 of 59
Phone: (215) 568-3100

49/59

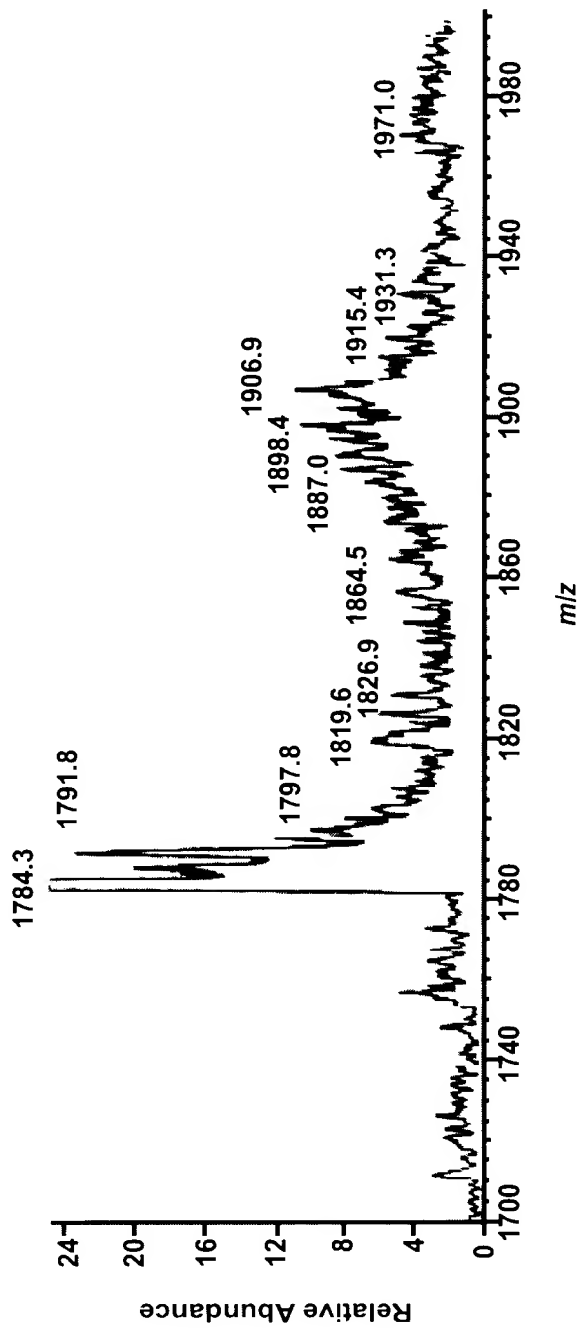


Figure 42B



50/59

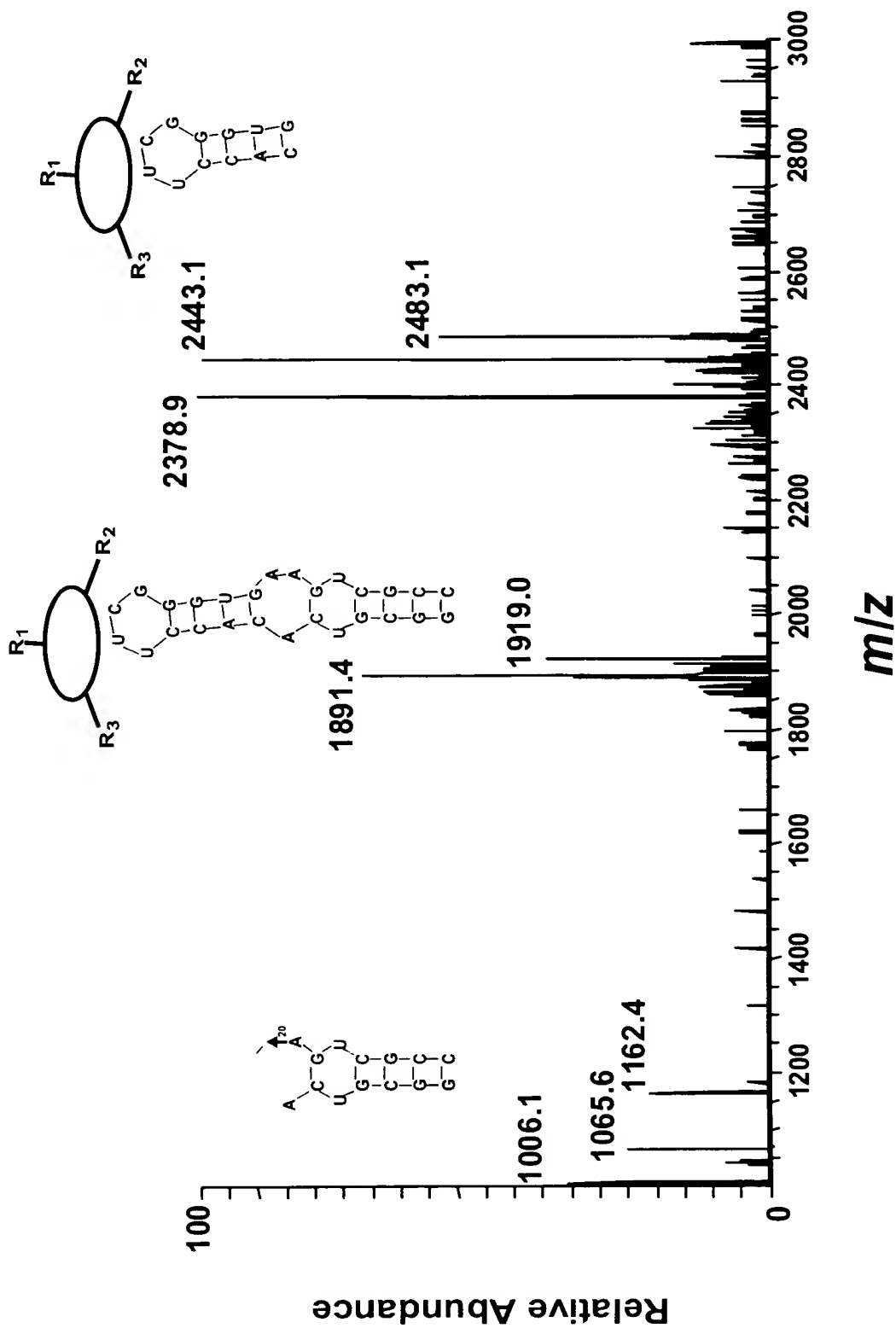


Figure 43

51/59

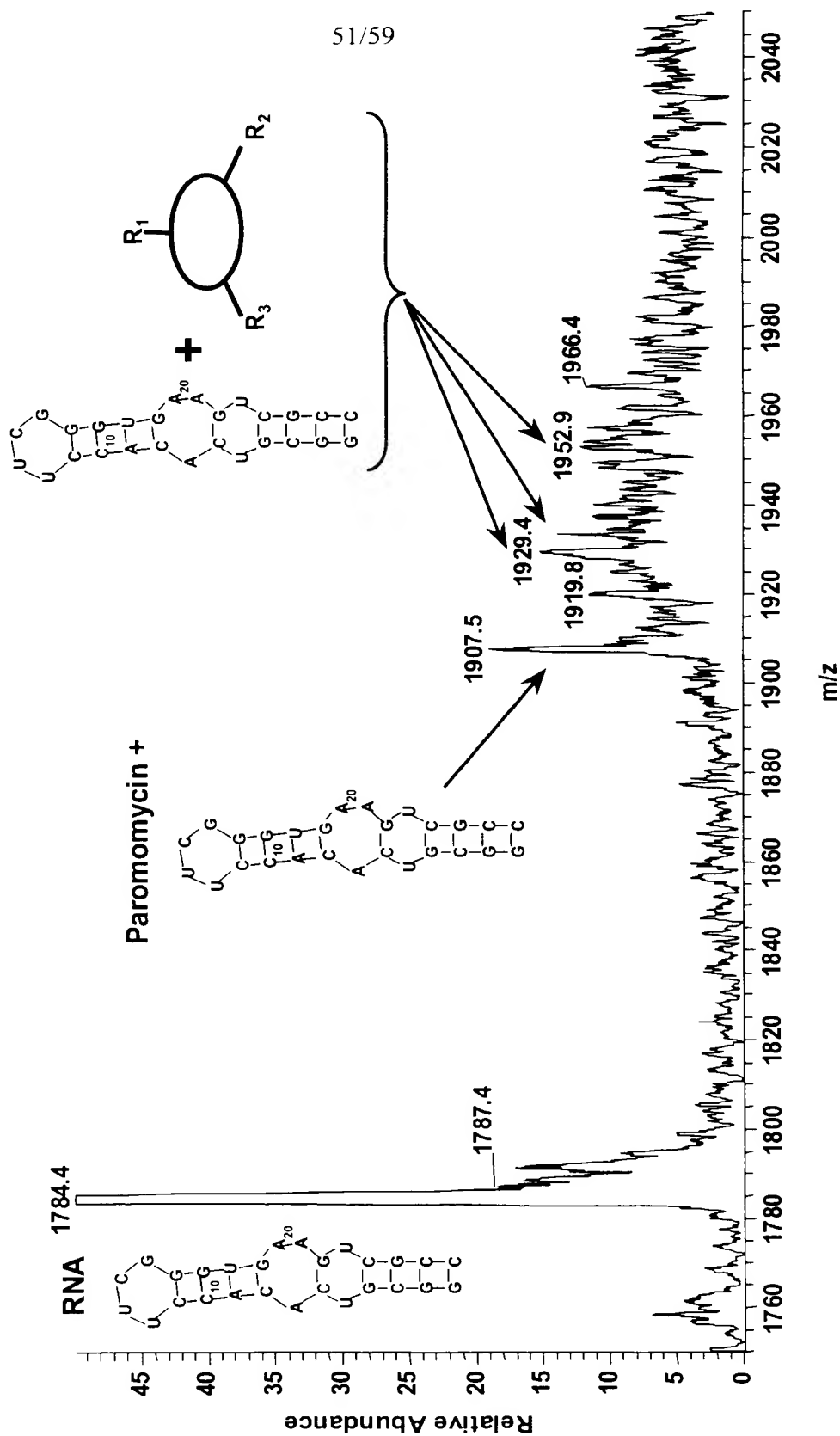


Figure 44



52/59

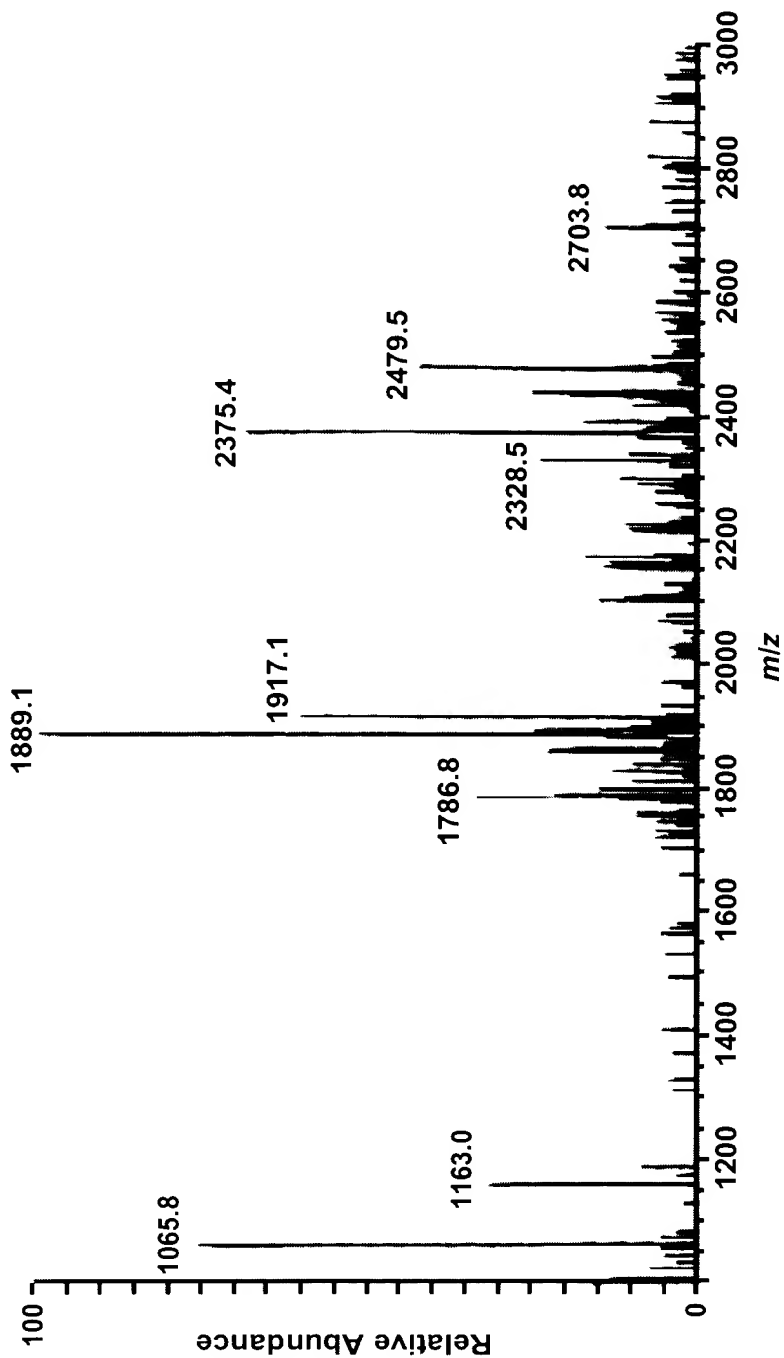


Figure 45

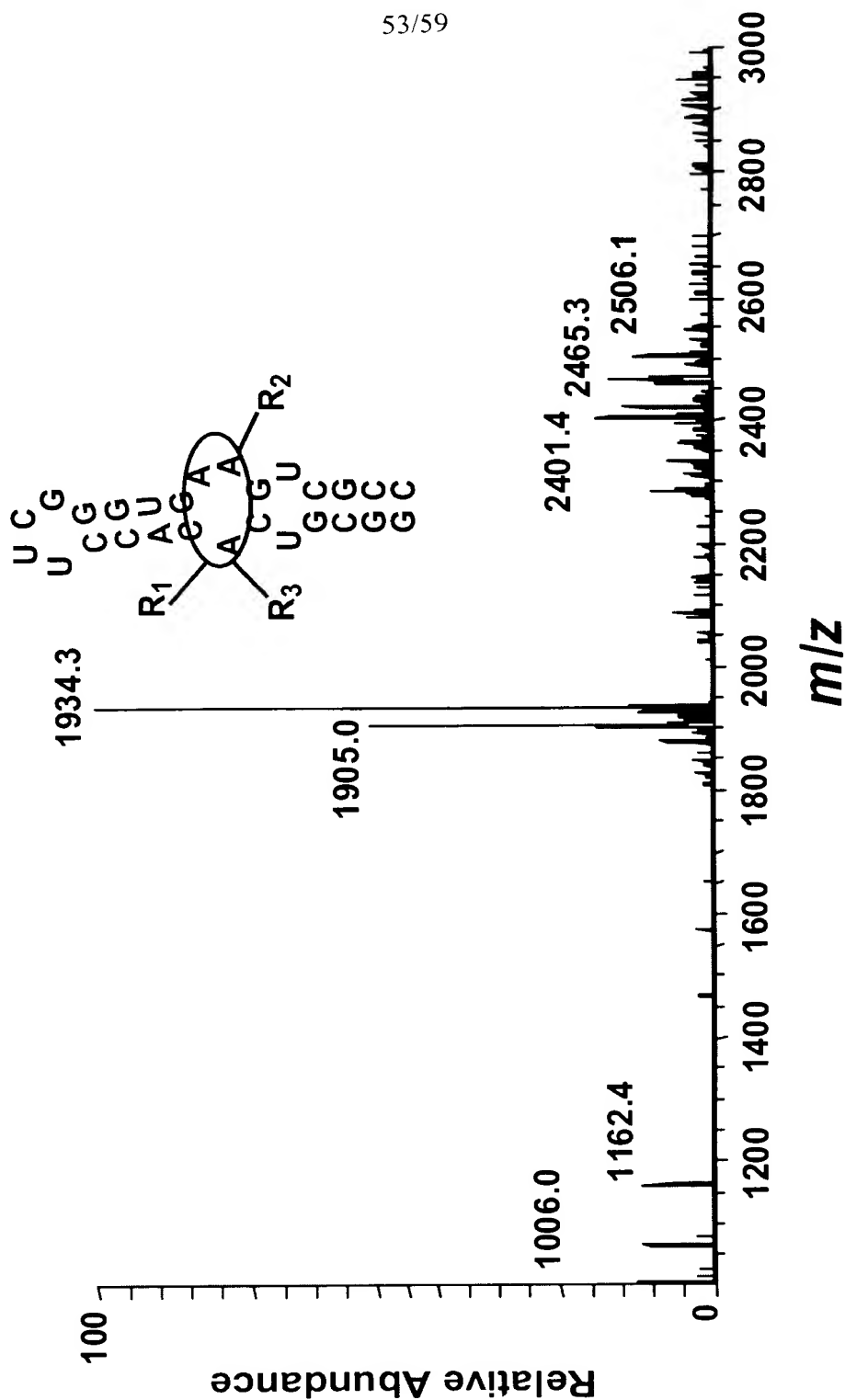


Figure 46